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EDITORIAL (for October 2022 issue of JTH)

The future of basic science research into a leading cause of disability and death

In June, our journal published a position paper[1] from the Basic Science Task Force of the Scientific and Standardization Committee (SSC) of the International Society on Thrombosis and Haemostasis (ISTH), who worked to identify research opportunities for basic science in hemostasis and thrombosis. These investigators noted, disturbingly, that "Funding directed toward discovery research in thrombosis and hemostasis has seen a significant reduction in the last 8–10 years. In the same period there has been a steady decline in the number of basic science abstracts submitted to the ISTH congresses." Here we reprint Figure 1 from their position paper, showing that, while submissions of clinical abstracts to the annual ISTH Congress (arguably the most important scientific meeting centering on hemostasis and thrombosis) have remained constant from 2007 to 2020, submissions of basic research abstracts to this meeting have decayed alarmingly.

Why be alarmed that basic science on this topic appears to be waning? Despite public health gains in recent decades, thrombotic diseases stubbornly remain one of the major causes of disability and death worldwide. Although ischemic heart disease and stroke are estimated to cause one in four deaths, the ISTH Steering Committee for World Thrombosis Day concluded that this statistic seriously under-counts the worldwide disease burden from thrombosis, particularly when venous thromboembolic diseases are included.[2,3] Thrombosis is also a major cause of death from cancer, and dysregulation of the blood clotting system contributes profoundly to death from disease states ranging from sepsis to trauma. And as the world has just witnessed, disorders of the blood clotting system play a profound role in the pathology of COVID-19. Given the wide variety of viruses already known to induce coagulopathies, one wonders what future pandemics have in store for us.

Currently available antithrombotic drugs were developed to diminish the risk of thrombosis in patients whose coagulation systems are largely intact—albeit with a balance tipped a bit more toward clotting than is desirable. These drugs were not developed for use in patients whose clotting systems are badly deranged, and none of them address the root causes of such derangement. Although conventional (broadly acting) anticoagulant drugs such as heparins show benefit in some COVID-19 patients,[4] the fact remains that we need a much better armamentarium of treatment modalities that selectively target specific aspects of the coagulation system. And to achieve that, we need a much better understanding of how the clotting system behaves at a mechanistic level in a wide variety of diseases that trigger coagulopathies.

Given the importance of the blood clotting system in so many disease states, and given the great societal burden of thrombotic and bleeding disorders, why would the amount of basic discovery research be declining over the past several years? As the SSC Task Force stated, one reason is that funding directed toward discovery research on this topic has fallen over the past decade, leading to reduced research in this area. This is something that the appropriate funding

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agencies could change as a matter of will. Another problem, frankly, is that discovery research is very hard to do, and gets harder every year! While the topic of blood clotting has benefited from decades of research, this has created a serious "knowledge burden"[5] that must be mastered by new investigators before they become competitive. As the journalist, Derek Thompson, succinctly summarized, "We are learning more about the world every year, but the more we learn about any subject, the harder it is to master all the facts out there and push the frontier of knowledge outward."[6] And as Thompson points out, the cumulative effects this "knowledge burden" also help explain why the average age of NIH research grant recipients has steadily and dramatically increased over recent decades (Figure 2).

How can we address this problem? The issue of declining funding in thrombosis and bleeding could be reversed by granting agencies. Personal experience has taught us, however, that many researchers outside our area view blood clotting as a very mature field—so much so, that some feel that everything important on this topic has already been discovered and that we are now filling in the minor details. Blood clotting is a mature field in the sense that there is a substantial "knowledge burden" to be mastered. But, as with most complex biological systems such as genetics and immunology, our understanding of blood clotting is still lacking many details to appreciate the integration of coagulation into physiologic and pathophysiologic states. So much remains to be discovered, especially regarding the myriad connections between blood clotting/fibrinolysis/platelets and inflammation, the immune system, virology, cancer—the list goes on and on. Funding agencies need to learn this lesson and focus more attention on reducing the enormous societal burden represented by thrombotic and bleeding disorders. We will not make further important treatment advances without supporting the discovery pipeline.

What about the issue of "knowledge burden"? This is a more vexing problem but one that needs to be tackled. Some granting agencies have instituted more generous paylines for early-stage investigators, and while this sends more research funds to younger investigators, it does not really address the knowledge burden issue. We call on all parties involved—learned societies like ISTH and the SSC, granting agencies, and individual researchers—to think collectively about how to address this problem and to take action. Overcoming the "knowledge burden" barrier is important not only to new investigators, but also to seasoned investigators in fields such as bioengineering, chemistry, and materials science, who would like to bring powerful approaches to tackling problems in our field, but who risk asking naïve research questions. Together, we all need to address the serious societal burden of thrombotic diseases, and this requires a redoubled emphasis on basic research on this important topic.

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FIGURE LEGENDS

FIGURE 1. Abstract submissions to the ISTH Congresses, showing linear regression analyses of clinical (gray) and basic science abstracts (red) submitted from 2007–2020. Reprinted with permission from Mutch et al.[1]

FIGURE 2. NIH R01 grant recipients who are younger than 35 or over 66, graphed from 1980 to 2014. (From https://nexus.od.nih.gov/all/2015/03/25/age-of-investigator/, accessed 5 Aug. 2022.)

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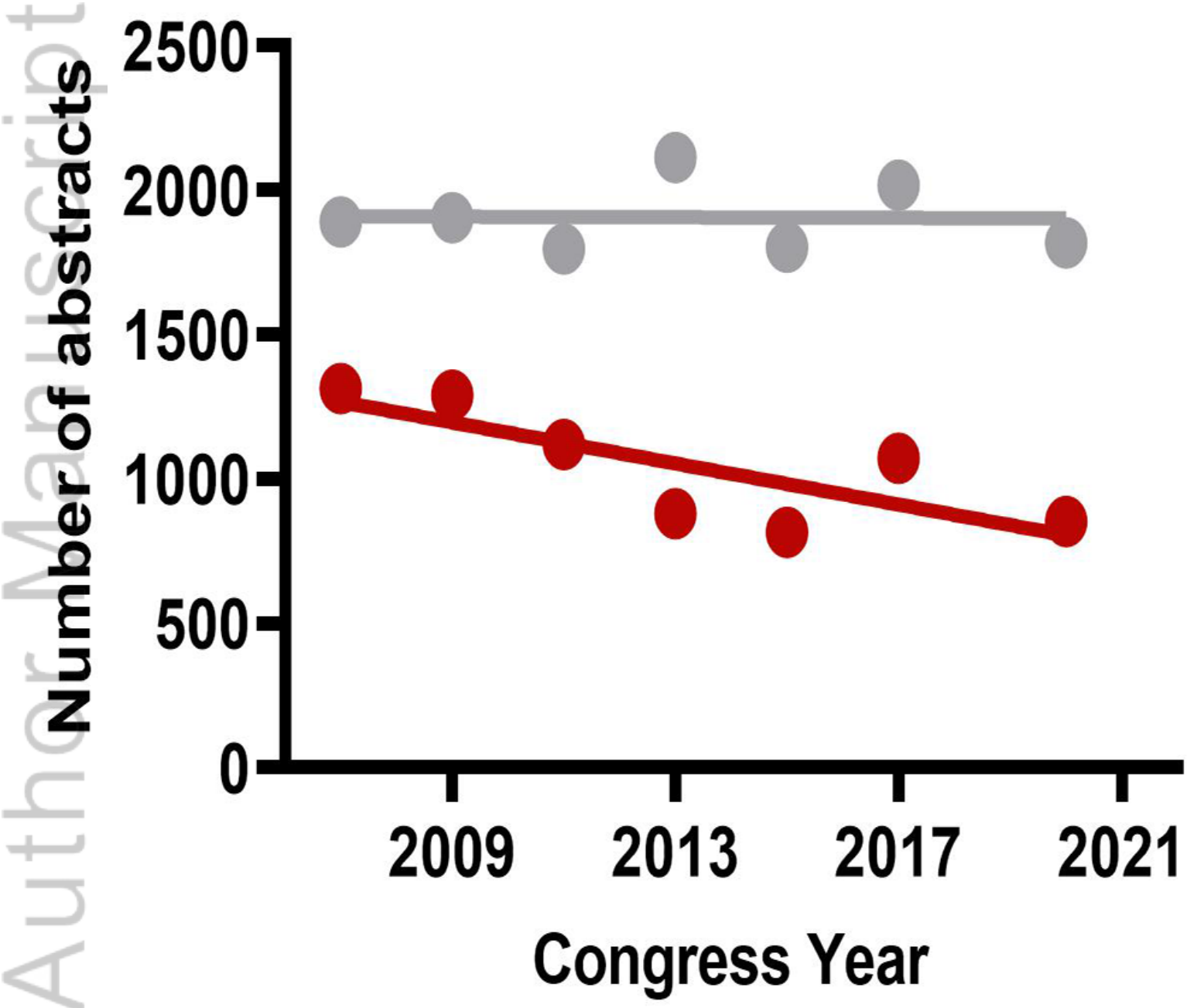


Figure_1.png

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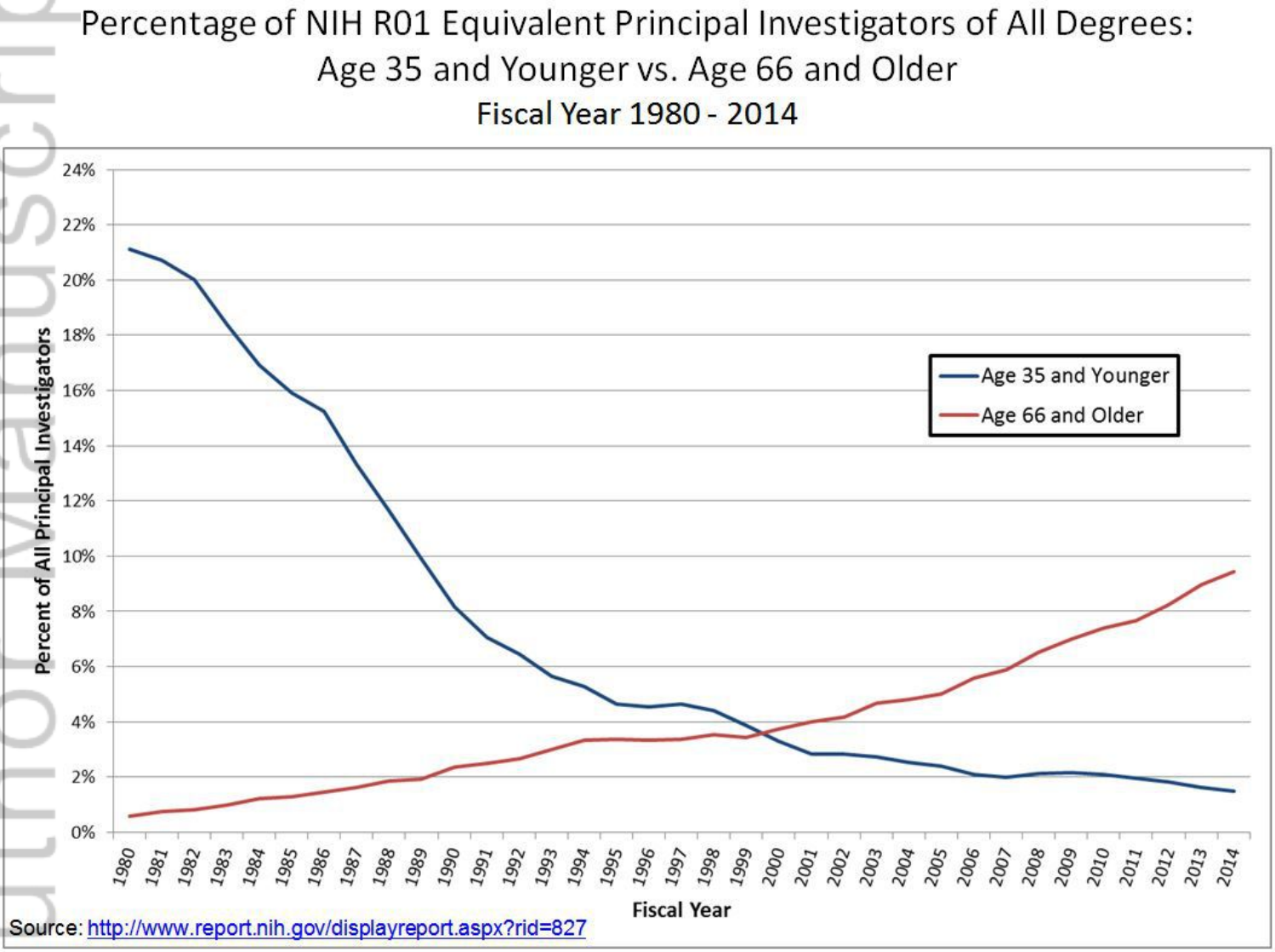


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